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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,725	12/21/2001	Sabine Flicker	25401-4	9787

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,725	FLICKER ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/3/05 has been entered.

2. Claims 25-46 are pending and are being acted upon in this Office Action.

3. The listing of references in the specification on page 21-24 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 34-35 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a timothy grass Phl p2 pollen allergen specific human IgE Fab for detection assay and for standardization of allergen extract using timothy grass Phl p2 pollen specific antibody comprising a heavy chain consisting of the amino acid sequence as shown in SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9, and a light chain consisting of the amino acid sequence as shown in SEQ I DNO: 10, SEQ ID NO: 11 or SEQ ID NO: 12, respectively, **does not** reasonably provide enablement for (1) any vaccine against any type I allergy comprising the any group 2 allergen specific human IgE Fab having a heavy chain consisting of an amino acid sequence as shown in SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID NO: 9 and a light chain consisting of an amino acid sequence as shown in SEQ ID NO: 10, SEQ ID NO: 11 or SEQ ID NO: 12, respectively, (2) a method for passive immunotherapy of any type I allergy comprising administering a Phl p2-specific IgE Fab as set forth in claim 35 and (3) any

vaccine against any type I allergen as set forth in claim 44. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The breath of the claims encompasses any a vaccine against any type I allergy using the human IgE Fab fragment and the corresponding complete antibody or the human IgE Fab fragment having the amino acid sequence of SEQ ID NO: 7-12 encoded by nucleic acid sequence of SEQ ID NO: 1-6 or the corresponding complete antibody.

The specification discloses only three timothy grass pollen Phl p2 allergen specific human IgE Fab fragments consisting of a heavy chain *and* a light chain wherein the heavy chain amino acid sequence consists of SEQ ID NO: 7 and the light chain amino acid sequence consists of SEQ ID NO: 10 or a heavy chain consisting of SEQ ID NO: 8 and a light chain consisting of SEQ ID NO: 11, or a heavy chain consisting of SEQ ID NO: 9 and a light chain consisting of SEQ ID NO: 12 for inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, (2) An Phlp2 specific antibody comprising the variable region comprising a heavy chain, *and* a light chain of a human IgG1 wherein the variable region comprises a heavy chain amino acid sequence is set forth in SEQ ID NO: 7 and the light chain amino acid sequence is set forth in SEQ ID NO: 10 or a heavy chain is set forth in SEQ ID NO: 8 and a light chain is set forth in SEQ ID NO: 11, or a heavy chain is set forth in SEQ ID NO: 9 and a light chain is set forth in SEQ ID NO: 12 for inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, and (3) a diagnostic reagent or a kit comprising said Phl p2 specific human IgE Fabs and/or said specific Phl p2 antibody mentioned above for detection assay (See pages 13 and 17-18). The specification further discloses all three IgE Fabs bound to the same recombinant fragment consisting of the N-terminal 64 amino acids of Phl p2. The specification discloses grafting the variable regions of the Phl p2 specific human IgE Fab fragments onto human IgG1 (page 3) for suppressing Phl p2

degranulation of basophiles. The specification discloses the claimed the recombinant phl p2-specific IgE Fabs may be useful for induction of a protective mucosal immunity (see page 16).

The specification does not teach any vaccine or any method of passive immunotherapy of any type I allergen using the claimed phl p2- specific IgE Fab or the corresponding complete antibody, any antibody comprising any combination of heavy and light chain, and any combination of IgE Fab and complete antibody. There is a lack of in vivo working example demonstrating that the claimed antibody Fab or complete antibody is effective as a vaccine against all type I allergy. Those of skill in the art recognize that in vitro assays and or cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon such as screening the effects of potential drugs. However, clinical correlations are generally lacking. The greatly increased complex city of the in vivo environment as compared to the very narrowly defined and controlled conditions for an in vitro assay does not permit a single extrapolation of vitro assays to human prevention of type I allergy with any reasonable degree of predictability.

Freshney et al teach culture environment lacks the several systemic components involved in homeostatic regulation in vivo. Without this control, cellular metabolism may be more constant in vitro than in vivo, but may not be truly representative of the tissue fro which the cells were derived (see enclosed pages in Culture of Animal Cells, in particular).

Denepoux et al teach various recombinant human monoclonal antibody Fabs to birch pollen allergen Bet v1 such as rBAB2 cannot interfere with allergic effector cells, mast cells, and basophils because they lack Fc region. However, this antibody whose binding to its allergen further enhances the binding of anaphylactic IgE and thus contributes to disease aggravation rather than reduce allergen-induced allergic reaction (see page 46, col. 1, abstract, in particular).

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

6. Claims 26-29, and 40 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "human IgG" in Claims 26, 28 and 40 represents a departure from the specification and the claims as originally filed. The specification discloses grafted variable regions of the IgE Fabs of the invention onto human IgG1 (see page 3, first paragraph).

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 25-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"**an** amino acid sequence" in claim 25 lines 2 and 3 and claim 45, lines 2 and 3 should have been "**the** amino acid sequence".

"group 2 allergen" in claims 25, 26, 39, 45 and 46 is ambiguous and indefinite because the specification discloses the human IgE-Fab is specific for timothy grass Phl p2 pollen allergen (see pages 4 and 8 of specification). The specification discloses the claimed human IgE Fabs cross-react with group 2 allergens selected from the group consisting of sweet vernal grass, rye grass, Kentucky Bluegrass, rye, wheat and oat (see page 13).

"A group 2 allergen specific human IgG comprising the variable regions of the IgE Fab of claim 45" is ambiguous and indefinite, it is suggested that claim 26 be amended to recite "An isolated timothy grass Phl p2 pollen allergen specific antibody comprising a human IgG1 and the variable regions of the IgE Fab of claim 45".

The "and/or the corresponding complete antibody" in claim 28 is indefinite because the IgG in claim 26 is already a complete antibody having the IgE Fab and human IgG. Thus, the term ", and/or the corresponding complete antibody" should be deleted.

The "**and**/or" in claim 32 is ambiguous and indefinite because the diagnostic reagent comprising the IgE Fab according to claim 45 or the corresponding complete antibody.

The "**and**/or" in claim 34 is ambiguous and indefinite because the specification does not teach a vaccine comprising the IgE Fab to claim 45 **and** the corresponding complete antibody.

"A group 2 allergen specific human IgG comprising the variable regions of the IgE Fab of claim 46" in claim 40 is ambiguous and indefinite because human IgG suddenly become IgE Fab. It is suggested that claim 40 be amended to recite "An isolated timothy grass Phl p2 pollen allergen specific antibody comprising a human IgG1 and the variable regions of the IgE Fab of claim 45".

"**Phl p2**-specific IgE Fab" in claims 36-38 does not correlate with "A **group 2 allergen** specific human IgE Fab" in claim 45.

"**and**/or" in claims 42 and 44 is ambiguous and indefinite because the specification does not teach a diagnostic reagent or a vaccine comprising the IgE Fab **and** the corresponding complete antibody.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

10. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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